EXHIBIT G

Drinking Water Advisory: Consumer Acceptability Advice and Health Effects Analysis on Methyl Tertiary-Butyl Ether (MtBE)

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U.S. Environmental Protection Agency
Office of Water
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LIST OF ABBREVIATIONS

DWEL	Drinking-Water-Equivalent-Level
HA	Health Advisory
kg	kilogram
L	liter
LOAEL	lowest-observed-adverse-effect level
MoE	margin of exposure
mg	milligram
MtBE	Methyl *tertiary*-butyl ether
MTD	Maximum Tolerated Dose
NOAEL	no-observed-adverse-effect level
OFW	odor free water
ppm	parts per million
μg	microgram
TBA	*tertiary*-butyl alcohol
VOC	volatile organic compound

FOREWORD

EPA's Human Health and Criteria Division (HECD)of the Office of Water developed an Advisory document for methyl *tertiary*-butyl ether (MtBE). This document is a non-regulatory document that analyses the currently available cancer and non-cancer data on this contaminant, as well as studies on its organoleptic (taste and odor) effects. The document is not a mandatory standard for action; however, this Advisory supersedes any previous drafts of drinking water advisories for this chemical.

There are many uncertainties and limitations associated with the toxicity data base for this chemical. The animal tests available to date (1997) were not conducted by exposing the animals to MtBE in drinking water, but rather by inhalation exposure or by introducing MtBE in oil directly to the stomach several times a week. Although useful for identifying potential hazards, limitations of the reported studies do not allow confident estimates of the degree of risk MtBE may pose to humans from low-level drinking water contamination. The toxicokinetic models are also limited in helping to perform an adequate extrapolation from the inhalation data to actual oral exposure from drinking water intake. Additional research is needed to resolve these issues before a more complete health advisory can be issued. Therefore, given the needs of the States and Regions for an Office of Water (OW) position on MtBE contamination of drinking water, HECD developed this "Drinking Water Advisory: Consumer Acceptability Advice and Health Effects Analysis on Methyl tertiary-Butyl Ether (MtBE)".

MtBE is generally unpleasant in taste and odor. Studies have been conducted on the concentrations of MtBE in drinking water at which individuals can detect the odor or taste of the chemical. This Advisory recommends that keeping levels of contamination in the range of 20 to 40 µg/L or below to protect consumer acceptance of the water resource would also provide a large margin of exposure (safety) from toxic effects.

The Advisory discusses the limitations of the current database for estimating a risk level for this contaminant in drinking water and characterizes the hazards associated with this route of exposure. This document has been peer reviewed both internally in the Agency and externally by experts in the field before its release to the public.

Note: In this Advisory, we use a risk characterization method called "Margin of Exposure (or safety)" which is different from traditional slope factors and reference doses (RfDs) as estimates of response to defined exposures. The "margin" is how far the environmental exposure of interest is from the lower end of the exposures at which animals or humans have shown some toxicity effect. The use of the margin of exposure approach is helpful in the following ways: 1. It allows for comparison of exposures associated with carcinogenic potential to those associated with non cancer health effects; 2. It provides the risk manager with a quick check to decide if the margin of exposure (safety) appears to be adequate even when mathematical extrapolation of

data from high to low dose cannot be done; and 3. It gives a better understanding of the degree of risk
associated with extrapolation of exposure data from animal studies to humans. For example, given the limited number of animals that usually can be used in experiments, they, at best, would detect a one in ten response (1×10^{-1}). A common procedure for carcinogens is to mathematically extrapolate from the exposure levels of animal tests to estimate risk at lower, environmental exposure levels. If the extrapolation is done as a straight line, a risk estimate of 1×10^{-6} generally corresponds to a margin of exposure of 100,000. If the true, but unknown, relationship is downward sloping, not a straight line, the risk at a 100,000 margin of exposure would be less than 1×10^{-6} and might be zero.

Health and Ecological Criteria Division
Office of Science and Technology
Office of Water

DRINKING WATER ADVISORY: CONSUMER ACCEPTABILITY ADVICE AND HEALTH EFFECTS ANALYSIS ON METHYL TERTIARY-BUTYL ETHER (MtBE)

EXECUTIVE SUMMARY

MtBE

MtBE is a volatile, organic chemical. Since the late 1970's, MtBE has been used as an octane enhancer in gasoline. MtBE promotes more complete burning of gasoline, thereby reducing carbon monoxide and ozone levels. Hence, MtBE is commonly used as a gasoline additive in localities that participate in the Winter Oxygenated Fuels program and/or the Reformulated Gasoline program to achieve or maintain compliance with the National Ambient Air Quality Standards. A limited number of instances of significant contamination of drinking water with MtBE have occurred due to leaks from underground and above ground petroleum storage tank systems and pipelines. MtBE, due to its small molecular size and solubility in water, moves rapidly into groundwater, faster than other constituents of gasoline. Public and private wells have been contaminated in this manner. Non-point sources, such as recreational watercraft, are most likely to be the cause of small amounts of contamination of surface waters. Air deposition through precipitation of industrial or vehicular emissions may also contribute to surface and ground water contamination. The extent of any potential for build-up in the environment from such deposition is uncertain.

This Advisory

The EPA Office of Water is issuing this Advisory to provide guidance for communities that may be exposed to drinking water contaminated with MtBE. The Advisory provides an analysis of current health hazard information and an evaluation of currently available data on taste and odor problems associated with MtBE contamination of water, as the latter affect consumer acceptance of the water resource. This Advisory does not recommend either a low-dose oral cancer risk number or a reference dose (RfD)[1] due to certain limitations of available data for quantifying risk. Guidance is given on the concentrations at which taste and odor problems likely would be averted, and how far these are from MtBE concentrations at which toxic effects have been seen

[1]Reference Dose is defined as "an estimate (with uncertainty spanning approximately an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects over a lifetime" (U.S. EPA, 1987).

in test animals. (The measure used is called a "margin of exposure" or MoE. For instance, if a measured concentration is 100,000 times less than the range of observation of effects in test animals, the margin of exposure is 100,000.

Conclusion and Recommendation

This Advisory recommends that keeping levels of contamination in the range of 20 to 40 µg/L or below to protect consumer acceptance of the water resource would also provide a large margin of exposure (safety) from toxic effects.

Taste and odor values are presented as a range, since human responses vary depending upon the sensitivities of the particular individual and the site-specific water quality conditions. These values are provided as guidance recognizing that water suppliers determine the level of treatment required for aesthetics based upon the customers they serve and the particular site-specific water quality conditions.

There are over four to five orders of magnitude between the 20 to 40 µg/L range and concentrations associated with observed cancer and noncancer effects in animals. There is little likelihood that an MtBE concentration of 20 to 40 µg/L in drinking water would cause adverse health effects in humans, recognizing that some people may detect the chemical below this range. It can be noted that at this range of concentrations, the margins of exposure are about 10 to 100 times greater than would be provided by an EPA reference dose (RfD) for noncancer effects. Additionally, they are in the range of margins of exposure typically provided by National Primary Drinking Water Standards under the Federal Safe Drinking Water Act to protect people from potential carcinogenic effects.

When adequate data become available, the Office of Water will publish another Advisory that includes quantitative estimates for health risks. This Advisory gives practical guidelines for addressing contamination problems and supersedes previous draft advisories. An Advisory does not mandate a standard for action.

Studies of MtBE Effects

There are no studies of effects on humans of long-term exposure to MtBE. All of the studies available for hazard assessment are laboratory animal studies.

Cancer effects. There are studies in rodents of the carcinogenicity of MtBE, as well as its metabolites, *tertiary*- butyl alcohol (TBA) and formaldehyde. The only oral cancer exposure study was conducted by Belpoggi and coworkers (1995). They gave MtBE to Sprague-Dawley rats (gavage in olive oil, at doses up to 1,000 mg/kg/day, 4 days per week for two years). Exposure caused a dose-related increase in the incidence of combined leukemia and lymphomas in the female rats and an increase in Leydig cell adenomas (benign testicular tumors) in the high-dose male rats. Use of this study to quantitatively assess risks from drinking water exposure has

limitations. There are potential differences in bolus versus drinking water exposures and possible vehicle (olive oil) effects. Moreover, there are few details on the actual reported tumor response data provided in the report. The lack of histopathological diagnoses and of individual animal data were reasons that the National Research Council panel recommended not using these tumor data in risk estimation until after a thorough peer review of this study.

There are two studies on the potential carcinogenicity of MtBE after inhalation exposure. Chun et al. (1992) administered MtBE to F344 rats at concentrations up to 8,000 ppm for 2 years. Exposure to MtBE caused an increase in the incidence of combined renal tubular adenomas and carcinomas, as well as Leydig cell adenomas of the testes in the male rats. The mild induction of α-2u-globulin by MtBE suggested that this protein may have played a role in male rat kidney tumorigenesis. The increase in the incidence of Leydig cell adenomas of the male rats in this study was not significantly different from the historical control value, although the difference from the concurrent controls was significant. Induction of Leydig cell tumors was also observed in Sprague-Dawley rats after oral exposure by gavage (Belpoggi et al., 1995) and lends support to the conclusion that the appearance of the tumor in both studies is treatment-related.

In the other inhalation study, Burleigh-Flayer et al. (1992) gave MtBE to CD-1 mice at concentrations up to 8,000 ppm for 18 months. This exposure was associated with a statistically significant increase in the incidence of hepatocellular carcinomas in male mice and of hepatocellular adenomas in female mice. , The Chun et al. (1992) and the Burleigh-Flayer et. al. (1992) studies currently cannot be used to calculate adequate hazard advisory values since we have no well-developed pharmacokinetic model for converting a chronic inhalation exposure of MtBE to an equivalent oral exposure. On-going work may support route-to-route extrapolation in the future.

The potential carcinogenicity of two metabolites of MtBE, TBA and formaldehyde has also been examined. In F344 rats, TBA has provided some evidence of carcinogenic activity in the males (but not in the female rats). In B6C3F1 mice, TBA exposure gave equivocal evidence of carcinogenic activity in male mice based on marginally increased incidence of thyroid tumors, and some evidence of carcinogenicity in female mice, based on an increased incidence of follicular cell hyperplasia and follicular cell adenomas of the thyroid gland. Data for carcinogenic activity is ambiguous for drinking water exposure to formaldehyde. A study by Soffritti et al. (1989) reported a dose-related increase in the incidence of leukemia and intestinal tumors in Sprague-Dawley rats. However, the experimental data presented in this publication was limited. Another drinking water study on formaldehyde by Til and coworkers (1989), using Wistar rats, found no evidence of carcinogenicity.

The carcinogenicity data support a conclusion that MtBE poses a potential for carcinogenicity to humans at high doses. The data do not support confident, quantitative estimation of risk at low exposure due to the limitations described above.

Noncancer toxicity. The collective evaluation of the reproductive and developmental studies of MtBE in animals indicate that inhalation exposure can result in maternal toxicity and adverse effects on the developing fetus (Bushy Run Research Center, 1991, 1989a, 1989b; Conaway et al., 1985). The fetal toxicity in the mouse developmental studies indicate that it may be more sensitive to inhalation of MtBE vapors than the rat or rabbit during gestation. However, it is possible to conclude that, at low concentrations, MtBE does not cause a developmental or reproductive hazard by inhalation in three different animal species. This also suggests that humans may not be at risk when exposed to very low concentrations of MtBE.

Effects on the kidney were observed in rats after oral and inhalation exposure to MtBE. The most pertinent noncancer toxicity data come from a 90-day oral exposure study in rats. The authors reported minimal effects on the kidneys at doses of 300 mg/kg/day and above (Robinson et al., 1990). In these animals, the MtBE was given once a day, as a bolus dose in corn oil. A single oral dose of MtBE in corn oil would not be considered representative of an intermittent exposure to MtBE that one would normally obtain from drinking water containing MtBE. In a longer term inhalation study, histopathological abnormalities were apparent (Chun et al., 1992). Uncertainties exist in quantifying risk from the oral data in the short-term study because of the bolus gavage dosing regime and the less-than-lifetime duration of the study. The uncertainty in extrapolating between routes affects the interpretation of the inhalation data.

The studies support a conclusion that MtBE can pose a hazard of noncancer effects to humans at high doses. The data do not support confident quantitative estimation of risk at low exposure.

Taste and Odor. Studies were conducted on the concentrations of MtBE in drinking water at which individuals respond to the odor or taste of the chemical. Human responses vary widely in this respect. Some who are sensitive can detect very low concentrations, others do not taste or smell the chemical even at much higher concentrations. Moreover, the presence or absence of other natural or water treatment chemicals can mask or reveal the taste or odor effects. Thus, variable preexisting water conditions around the country will increase variability in the acceptability of MtBE's presence in drinking water.

The studies have not been extensive enough to completely describe the extent of human variability, or to establish a population threshold of response. Nevertheless, the available studies allow a conclusion that keeping concentrations in the range of 20 to 40 micrograms per liter (µg/L) of water or below will likely avert unpleasant taste and odor effects, recognizing that some people may detect the chemical below this range.

Characterization Summary

Section 7.0 on hazard and dose response characterization summarizes the MtBE data. In this section, a table (Table 1) presents the margins of exposure comparing animal effects and human taste and odor data.